Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering to a mammalian subject having an abnormal brain region an agonist of ~~a calcium-activated or~~ an ATP-sensitive potassium channel, ~~the agonist being other than bradykinin or a bradykinin analog,~~ under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and administering to the subject simultaneously or substantially simultaneously with the agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

2. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke, or ischemia.

3. (currently amended) The method of Claim 1, wherein the abnormal brain region is ~~a region of benign or malignant~~ tumor tissue.

4. (currently amended) The method of Claim 1, wherein the potassium channel agonist is ~~NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein,~~ minoxidil~~, pinacidil, cromakalim, or levcromakalim~~.

5. (currently amended) The method of Claim 1, wherein said mammal is a human~~, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit~~.

6. (currently amended) The method of Claim 1, wherein the medicant is a therapeutic cytotoxic agent~~, protein, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody,~~

~~adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, or diagnostic agent~~.

Claim 7-10 cancelled.

11. (previously pending) The method of Claim 1, wherein administering the agonist is by intravenous or intra-arterial infusion or injection.

12. (previously pending) The method of Claim 1, wherein administering the agonist is by intracarotid infusion or injection.

13. (previously pending) The method of Claim 1, wherein the agonist is administered to the mammalian subject by a bolus injection.

14. (previously pending) The method of Claim 1, wherein the agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

15. (previously pending) The method of Claim 14, wherein the agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

16. (previously pending) The method of Claim 1, wherein the agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu g\ kg^{-1}\ min^{-1}$ for up to about 30 minutes.

17. (previously pending) The method of Claim 16, wherein the agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu g\ kg^{-1}\ min^{-1}$.

18. (currently amended) A method of selectively delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering to a mammalian subject having an abnormal brain region an agonist of ~~a calcium-activated or~~ an ATP-sensitive potassium channel~~, the agonist being other than bradykinin or a bradykinin analog,~~ under

conditions and in an amount sufficient to increase potassium flux through ~~a calcium-activated or~~ an ATP-sensitive potassium channel in an endothelial cell membrane of a capillary or arteriole delivering blood to cells of the abnormal brain region, whereby the capillary or arteriole is made more permeable to the medicant; and administering to the subject simultaneously or substantially simultaneously with the agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

Claims 19-96 canceled.

97. (currently amended) A pharmaceutical composition comprising a combination of an agonist of ~~a calcium-activated or~~ an ATP-sensitive potassium channel, ~~the agonist being other than bradykinin or a bradykinin analog,~~ formulated in a pharmaceutically acceptable solution together with a therapeutic cytotoxic agent ~~medicant~~ for delivery by intravascular infusion or injection into a mammal.

98. (original) The pharmaceutical composition of Claim 97, wherein the ~~solution is formulated to deliver a dose rate~~ agonist is present in an amount of about 0.075 to 1500 micrograms per kilogram body ~~mass in a pharmaceutically acceptable fluid volume over a period of up to thirty minutes~~.

99. (original) The pharmaceutical composition of Claim 97, wherein the ~~solution is formulated to deliver a dose rate~~ agonist is present in an amount of about 0.075 to 150 micrograms per kilogram body ~~mass in a pharmaceutically acceptable fluid volume over a period of up to thirty minutes~~.

100. (currently amended) The pharmaceutical composition of Claim 97, wherein the agonist is ~~NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein,~~ minoxidil~~, pinacidil, cromakalim, or leveromakalim~~.

Claims 101-105 canceled.

106. (original) The pharmaceutical composition of Claim 97, further comprising a buffer solution pharmaceutically acceptable for intravascular infusion into a mammal.

107. (original) The pharmaceutical composition of Claim 106, wherein the buffer solution is phosphate buffered saline.

108. (currently amended) A kit for enhancing the delivery of a medicant to an abnormal brain region, comprising: an agonist of a ~~calcium-activated or~~ an ATP-sensitive potassium channel~~, the agonist being other than bradykinin or a bradykinin analog;~~ and instructions for using the agonist for enhancing the delivery of a medicant to an abnormal brain region by increasing the permeability of a capillary or arteriole delivering blood to cells of the abnormal brain region.

109. (currently amended) The kit of Claim 108, wherein the potassium channel agonist is ~~NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein,~~ minoxidil, ~~pinacidil, cromakalim, or levcromakalim~~.

110. (new) The method of Claim 1, wherein the agonist is minoxidil sulfate.

111. (new) The method of Claim 1, wherein the agonist is diazoxide.

112. (new) The method of Claim 1, wherein the agonist is pinacidil.

113. (new) The method of Claim 1, wherein the agonist is cromakalim.

114. (new) The method of Claim 1, wherein the agonist is levcromakalim.

115. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by stroke.

116. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by ischemia.

117. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury or trauma.

118. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by infection.

119. (new) The method of Claim 1, wherein the abnormal brain region is a region of benign tumor tissue.

120. (new) The method of Claim 1, wherein the abnormal brain region is a region of malignant tumor tissue.

121. (new) The method of Claim 1, wherein the abnormal brain region includes a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

122. (new) The method of any of Claim 1, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

123. (new) The method of any Claim 1, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

124. (new) The method of Claim 1, wherein the medicant is a protein.

125. (new) The method of Claim 1, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

126. (new) The method of Claim 1, wherein the medicant is a cytokine, cytokine antagonist, or cytokine agonist.

127. (new) The method of Claim 1, wherein the medicant is an interferon.

128. (new) The method of Claim 1, wherein the medicant is interleukin-2.

129. (new) The method of Claim 1, wherein the medicant is transforming growth factor-β.

130. (new) The method of Claim 1, wherein the medicant is a tumor necrosis factor-α.

131. (new) The method of Claim 1, wherein the medicant is an antimicrobial agent or an antibiotic.

132. (new) The method of Claim 1, wherein the medicant is an immunotoxin or immunosuppressant.

133. (new) The method of Claim 1, wherein the medicant is a boron compound.

134. (new) The method of Claim 1, wherein the medicant is an ischemia-protective agent.

135. (new) The method of Claim 134, wherein the ischemia-protective agent is N-methyl-D-aspartate (NMDA) receptor antagonist.

136. (new) The method of Claim 1, wherein the medicant is an adrenergic agent.

137. (new) The method of Claim 1, wherein the medicant is an anticonvulsant.

138. (new) The method of Claim 1, wherein the medicant is an anti-trauma agent.

139. (new) The method of Claim 1, wherein the medicant is cisplatin or carboplatin.

140. (new) The method of Claim 1, wherein the medicant is methotrexate.

141. (new) The method of Claim 1, wherein the medicant is 5-flouroouracil.

142. (new) The method of Claim 1, wherein the medicant is amphotericin.

143. (new) The method of Claim 1, wherein the medicant is daunorubicin.

144. (new) The method of Claim 1, wherein the medicant is doxorubicin.

145. (new) The method of Claim 1, wherein the medicant is vincristine.

146. (new) The method of Claim 1, wherein the medicant is vinblastine.

147. (new) The method of Claim 1, wherein the medicant is busulfan.

148. (new) The method of Claim 1, wherein the medicant is chlorambucil.

149. (new) The method of Claim 1, wherein the medicant is cycloposhamide.

150. (new) The method of Claim 1, wherein the medicant is melphalan.

151. (new) The method of Claim 1, wherein the medicant is ethyl ethanesulfonic acid.

152. (new) The method of Claim 1, wherein the medicant is a diagnostic agent.

153. (new) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering simultaneously or substantially simultaneously to a mammalian subject having an abnormal brain region (i) minoxidil or minoxidil sulfate and (ii) a medicant, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

154. (new) A method of delivering a therapeutic cytotoxic agent to an abnormal brain region in a mammalian subject, comprising: administering simultaneously or substantially simultaneously to a mammalian subject having an abnormal brain region (i) minoxidil or

minoxidil sulfate and (ii) a therapeutic cytotoxic agent, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

155. (new) The method of Claim 153, wherein the medicant is cisplatin or carboplatin.

156. (new) The method of Claim 153, wherein the medicant is methotrexate.

157. (new) The method of Claim 153, wherein the medicant is 5-flourouracil.

158. (new) The method of Claim 153, wherein the medicant is amphotericin.

159. (new) The method of Claim 153, wherein the medicant is daunorubicin

160. (new) The method of Claim 153, wherein the medicant is doxorubicin.

161. (new) The method of Claim 153, wherein the medicant is vincristine or vinblastine.

162. (new) The method of Claim 153, wherein the medicant is busulfan.

163. (new) The method of Claim 153, wherein the medicant is chlorambucil.

164. (new) The method of Claim 153, wherein the medicant is cyclophosphamide.

165. (new) The method of Claim 153, wherein the medicant is melphalan.

166. (new) The method of Claim 153, wherein the medicant is ethyl ethanesulfonic acid.

167. (new) The pharmaceutical composition of Claim 97, wherein the agonist is mioxidil.

168. (new) The pharmaceutical composition of Claim 97, wherein the agonist is minoxidil sulfate.

169. (new) The pharmaceutical composition of Claim 97, wherein the agonist is cromakalim.

170. (new) The pharmaceutical composition of Claim 97, wherein the agonist is pinacidil.

171. (new) The pharmaceutical composition of Claim 97, wherein the agonist is diazoxide.

172. (new) The pharmaceutical composition of Claim 97, wherein the agonist is levcromakalim.

173. (new) The pharmaceutical composition of Claim 97, wherein the therapeutic cytotoxic agent is cisplatin or carboplatin.

174. (new) The pharmaceutical composition of Claim 97, wherein the therapeutic cytotoxic agent is 5-fluorouracil.

175. (new) The pharmaceutical composition of Claims 97, wherein the therapeutic cytotoxic agent is methotrexate.

176. (new) The pharmaceutical composition of Claim 97, wherein the therapeutic cytotoxic agent is amphotericin.

177. (new) The pharmaceutical composition of Claim 97, wherein the therapeutic cytotoxic agent is daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

178. (new) A pharmaceutical composition comprising a combination of an agonist of an ATP sensitive potassium channel formulated together in a pharmaceutically acceptable solution together with a drug for delivery by intravascular infusion or injection, wherein the drug is a protein, antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binding antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anti-convulsant, anti-trauma agent or diagnostic agent.

179. (new) The pharmaceutical composition of Claim 178, wherein the drug is a protein.

180. (new) The pharmaceutical composition of Claim 178, wherein the drug is an antimicrobial agent.

181. (new) The pharmaceutical composition of Claim 178, wherein the drug is a cytokine.

182. (new) The pharmaceutical composition of Claim 178, wherein the cytokine is interleukin-2.

183. (new) The pharmaceutical composition of Claim 181, wherein the cytokine is transforming growth factor-β.

184. (new) The pharmaceutical composition of Claim 191, wherein the cytokine is tumor necrosis factor-α.

185. (new) The pharmaceutical composition of Claim 178, wherein the drug is an interferon.

186. (new) The pharmaceutical composition of Claim 178, wherein the drug is a monoclonal antibody or antigen-binding antibody fragment.

187. (new) The pharmaceutical composition of Claim 178, wherein the drug is an immunotoxin or immunosuppressant.

188. (new) The pharmaceutical composition of Claim 178, wherein the drug is an ischemia-protective agent.

189. (new) The pharmaceutical composition of Claim 189, wherein the ischemia-protective agent is N-methyl-D-aspartate (NMDA) receptor antagonist.

190. (new) The pharmaceutical composition of Claim 178, wherein the drug is an adrenergic agent.

191. (new) The pharmaceutical composition of Claim 178, wherein the drug is a boron compound.

192. (new) The pharmaceutical composition of Claim 178, wherein the drug is an anti-convulsant,

193. (new) The pharmaceutical composition of Claim 178, wherein the drug is an anti-trauma agent.

194. (new) The pharmaceutical composition of Claim 178, wherein the drug is a diagnostic agent

195. (new) The kit of Claim 108, wherein the agonist is minoxidil sulfate.

196. (new) The kit of Claim 108, wherein the agonist is pinacidil.

197. (new) The kit of Claim 108, wherein the agonist is cromakalim.

198. (new) The kit of Claim 108, wherein the agonist is levcromakalim.

199. (new) The kit of Claim 108, wherein the agonist is diazoxide.